DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

FEB 17 1999

NDA 20-145/S-011
20-225/S-007

Schering Corporation
Attention: Joseph F. Lamendola, Ph.D.
2000 Galloping Hill Road
Kenilworth, NJ 07033

Dear Dr. Lamendola:

Please refer to your supplemental new drug applications dated January 26, 1999 (NDA 20-145) and January 19, 1999 (NDA 20-225) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nitro-Dur (nitroglycerin) Transdermal Infusion System (NDA 20-145) and Imdur (isosorbide mononitrate) Tablets (NDA 20-225).

This supplemental new drug applications provide for final printed labeling revised by the addition of the following paragraph in bold print as the first warning under **WARNINGS:**

> Amplification of the vasodilatoty effects of Imdur/Nitro-Dur by sildenafil can result in severe hypotension. The time course and dose dependence of this interaction have not been studied. Appropriate supportive care has not been studied, but it seems reasonable to treat this as a nitrate overdose, with elevation of the extremities and with central volume expansion.

We have completed the review of these supplemental applications and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the final printed labeling included in your January 26 and 19, 1999 submissions. Accordingly, the supplemental applications are approved effective on the date of this letter.

We remind you that you must comply with the requirements for approved NDAs set forth under 21 CFR 314.80 and 314.81.

In addition, at your next printing, please change “children” to “pediatric patients” in the **Pediatric Use** statement. Supplemental applications need not be submitted to implement this change. It should, however, be reported in your annual reports.

If you have any questions, please contact:

Mr. Gary Buehler
Regulatory Health Project Manager
(301)594-5332

Sincerely yours,

Raymond J. Lipicky, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
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